SITUATIONAL CHEMICAL EXPOSURE STUDIES PROVIDE HUMAN METABOLISM AND URINE CLEARANCE DATA FOR CHLORPYRIFOS (C), DIMETHOATE (D) AND MALATHION (M)

30th Annual Society of Toxicology Meeting
February 26 - March 1, 1991
Dallas, Texas

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ABSTRACT

Organophosphorus insecticide exposures were monitored by measuring alkyl phosphate esters (APs) in urine. Situational studies are unscheduled opportunities for monitoring that provide human metabolic and kinetic data concerning chemical exposures. Exposures included Chlorpyrifos (C) following indoor fogging, Dimethoate (D) food residues, and Malathion (M) date dusting (MDL 25 ppb). Urines were collected for up to 4 days and analyzed for corresponding dialkyl-,dialkylthio-, and dialkyldithio phosphates plus D/oxon and M mono-/diacid. Cumulative metabolites were plotted as f (time) and sigma minus analysis used to estimate half-life. Urine clearance of similar self-administered oral and dermal dosages was also measured. (1) 2 adults treated their 825 ft_2 apartment with 6 home foggers containing C and followed normal weekend schedules for the following 48h. Urine from the corresponding period contained no APs (MDL <50 ug/person). (2) Peas containing violative levels of D (16 vs 2 ppm tolerance)

were ingested (ca. 0.1 mg/kg). Clearance of APs was rapid $t_{1/2}$ 2-3h and consistent with oral and dermal findings. (3) M dust exposures of an observer in a date garden resulted in rapid appearance (4-5h) of APs and M/acids. Availability of M was greater than expected. Clearance was rapid ($t_{1/2}$ 3-5h). Exposure assessments may be augmented by situational studies which represent human experience rather than hypothetical worst-case scenarios.

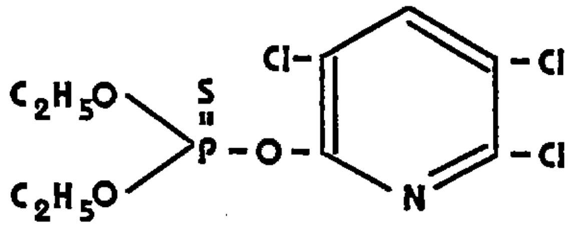
Situational Chemical Exposure Studies represent important opportunities to index the magnitude of human exposure under actual use conditions. Although yielding limited data, **SCES** may permit early evaluation of assumptions and critical exposure factors.

RESIDENTS FOLLOWING INDOOR CHLORPYRIFOS FOGGING

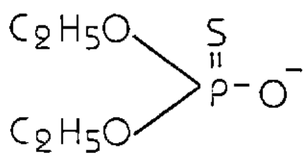
Indoor foggers are alleged to produce illness because of excessive pesticide exposures (Berteau *et al.*, 1985, and 1989), and reevaluation is occurring in California and within other regulatory agencies. Exposure data are limited but indoor exposures have been studied recently using humans in whole body dosimetry clothing (Ross *et al.*, Chemosphere 1990). These carefully controlled studies are essential to understanding basic processes that drive and limit pesticide transfer from treated surfaces to humans.

Situational chemical exposure studies can provide critical information about the magnitude of pesticide absorbed following normal use of a chlorpyrifos fogger.

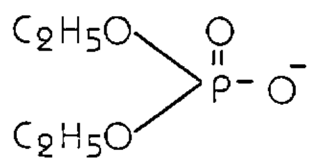
Two adults (male 22 y, female 21 y) treated their apartment with six home-foggers. They left the premises for two hours and ventilated by opening doors and windows for 30 minutes before reentering and assuming normal indoor weekend activities. Each person spent more than 20 hours each day there-after inside the apartment, and collected total urinary output.



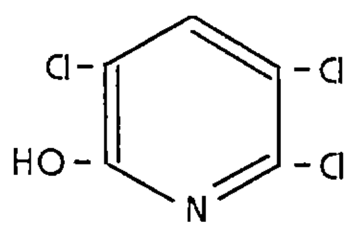
Chlorpyrifos



DETP



DEP



Pyridinol

METABOLITES

Urine monitoring commenced with a preexposure sample at about 0800 on Day One and continued for 48 hours. Individual voids were analyzed for dimethyl phosphate esters (MDL<50 μg/person). Neither set of urine (1000-1500 ml/d) contained detectable dimethyl phosphate esters. The pyridinol was not measured.

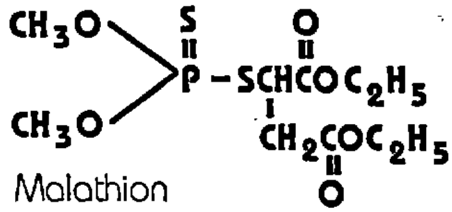
FATE OF 1 MG/KG DERMAL DOSAGE

Applied	Recovered	% Recovered
150 mg	$(C_2H_5O)_2PSO$ $(C_2H_5O)_2POO$	<1%

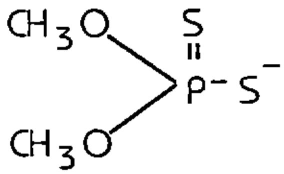
Chlorpyrifos is poorly absorbed via the dermal route. Nolan *et al.* have estimated dermal absorption of chlorpyrifos to be less than 5%. In our own pilot studies absorption could not be measured when $CHCl_3$ was used as a vehicle and was less than 1% when applied in Dowanol DPM (dipropylene glycol monomethyl ether). The high boiling solvent likely prolongs the contact between the stratum corneum and chlorpyrifos. Chlorpyrifos apparently has low potential for dermal absorption in humans who contact residues following use of foggers for flea control.

DATE DUSTERS AND HARVESTERS: MALATHION

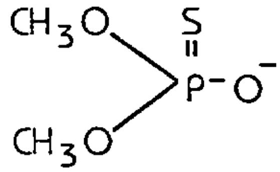
Date dusters and harvesters may be exposed to 5% malathion dust daily for up to 3 months in late summer and fall. There has been substantial concern about chemical hazards in their very dusty work environment. Pilot studies were conducted to characterize the work tasks and to estimate the magnitude of the worker's malathion exposure. Dermal and oral studies of malathion metabolism and excretion were available. Five metabolites were measured in urine of an observer and some workers to evaluate biomonitoring potential and dosimetry.



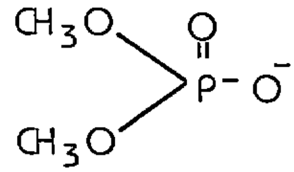
Malathion



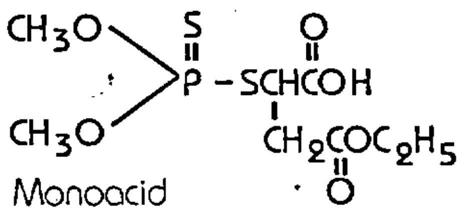
DMDTP



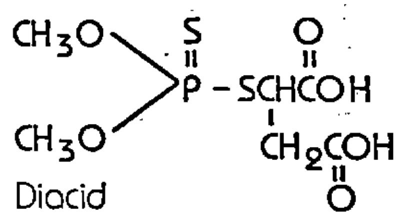
DMTP



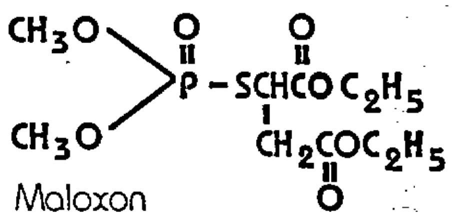
DMP



Monoacid

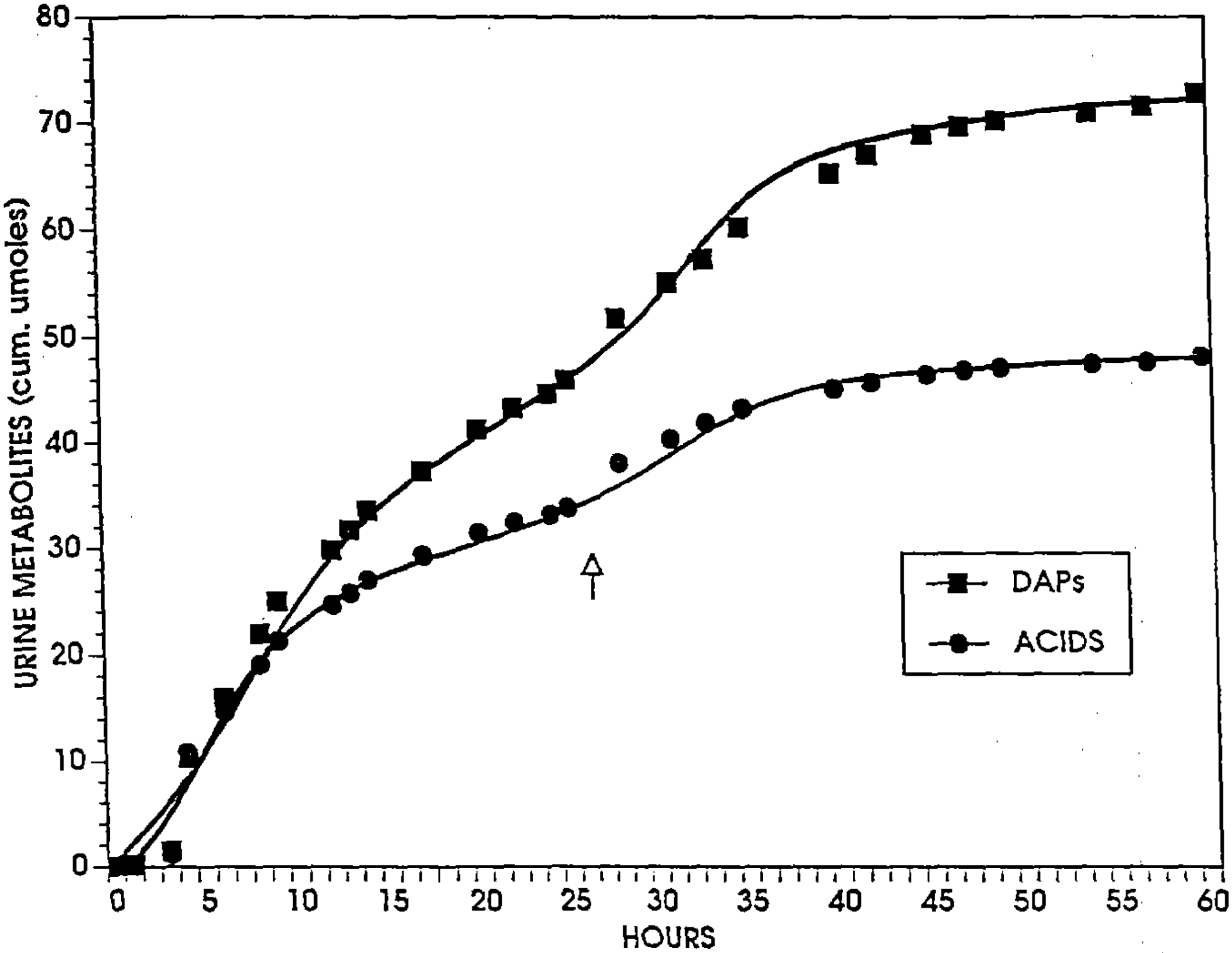


Diacid



Maloxon

Observer exposures (ca. 2h) occurred on successive days during application of 5% malathion dust (80 lbs./A). A shower was taken after 5-6 hours. Excretion continued throughout the first day. An incremental increase of lower magnitude was observed following the second day's exposure. Worker and observer exposures were of similar magnitude and thus the more complete observer data are useful for establishment of a biomonitoring program.



GROUND BOOM APPLICATOR OBSERVER

Conventionally an estimate of absorbed dose would be based upon Potential Dermal Exposure, *i.e.* the amount of malathion intercepted by outer clothing (shirt, jeans, socks). If PDE is factored by a 0.1 clothing penetration factor and 0.1 dermal absorption the Estimated Absorbed Dose can be calculated.

Note that this procedure substantially underestimates the Measured Absorbed Dose in these two cases. A likely source of error is inhaled and/or ingested malathion dust. Series of worst case estimates using passive dosimetry alone would likely obscure the possible importance of air borne malathion and could result in inappropriate risk management measures.

SITUATIONAL CHEMICAL EXPOSURE MONITORING: MALATHION METABOLITES FROM DATE DUSTING AND HARVEST

	DMP	DMTP	DMDTP	MCA	DCA	TOTAL
APPLICATOR OBSERVER[a]						
1 10/9 Ground	4	56	13	29	19	121
2 9/19 Ground	1	31	3	13	9	57
3 9/14 Boom	2	12	4	6	4	28
TOTAL (µmoles)		99 (48%)		48 (23%)		206
GROUND APPLICATORS (10/9/90)[b]						
A	4	93	9	48	28	182
B	4	109	13	58	26	210
C	1	54	6	26	8	95
TOTAL (µmoles)		256 (53%)		132 (27%)		487
HARVESTER OBSERVER[c]						
3 11/7	5	98	32	60	33	278
4 11/8	2	4	0.4	0.8	0.7	9
TOTAL (µmoles)		102 (36%)		61 (21%)		287
HARVESTERS						
3-AA 11/7[d]	2	29	10	19	4	64
4-BB	1	11	2	9	2	25
5-CC	1	20	3	19	3	46
6-DD	5	52	26	46	12	138
7-EE	4	41	15	27	13	100
8-FF	5	53	14	40	14	126
TOTAL (µmoles)		206 (41%)		160 (32%)		499
1-HSA 11/8[e]	0.1	2	0.2	1	0.5	4
2-HSB	0.2	3	0.4	2	1	8
3-HSC	0.2	4	0.5	2	1	8
4-HSD	0.3	4	0.5	2	1	8
5-HSE	0.3	6	2	4	2	14
6-HSF	0.4	7	2	4	2	15
TOTAL (µmoles)		26 (46%)		15 (26%)		57

[a]Exposure: 2 h, dusty environment — Urine collection: total, 72 h
[b]Exposure: 2-3 h, dusty environment — Urine collection: single, mid-shift
[c]Exposure: 1h date harvest, dusty environment — Urine collection: total, 48 h
[d,e]Exposure: 4h date harvest, dusty environment — Urine collection: single, mid-shift

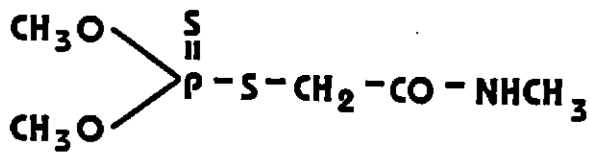
In this series of pilot studies, conducted with the cooperation of the union workers' physician, the observer was monitored throughout. Note that the Applicator and Harvester Observer urine samples (complete 24 h) contained malathion metabolites in amounts similar to those of the mid-shift urines of Ground Applicators and Harvesters. These numbers may not be reliably used to estimate total exposure since only partial sampling was possible. (Key urinary metabolites are malathion monoacid and dimethylthiophosphate.) The results show the utility of monitoring the observer and workers to help establish a future monitoring program.

DIMETHOATE RESIDUES IN SUGAR PEAS

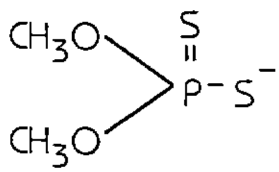
Illegal residues of dimethoate insecticide were detected on sugar peas during routine monitoring in California. Residues ranged from 12 ppm to 39 ppm; the food tolerance is 2 ppm. Regulators recalled sugar peas in the channels of trade and issued a health advisory concerning potential toxicity.

Illegal food residues of organophosphate insecticides are often erroneously assigned health significance due to serial conservative assumptions related to human consumption, residue stability during shipping, storage and food preparation, and limited acute data on health effects.

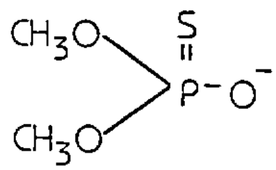
In this situation large amounts (1.1 kg) of sugar peas that contained violative residues (16 ppm dimethoate; 17.3 mg) were available. The peas were divided into eight portions and consumed raw <u>in</u> <u>toto</u> during a five-hour period. RBC cholinesterase was measured and urinary dimethoate metabolites were analyzed in successive samples collected during the 48-hour study period.



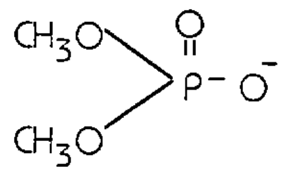
Dimethoate



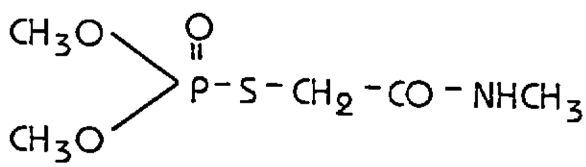
DMDTP



DMTP

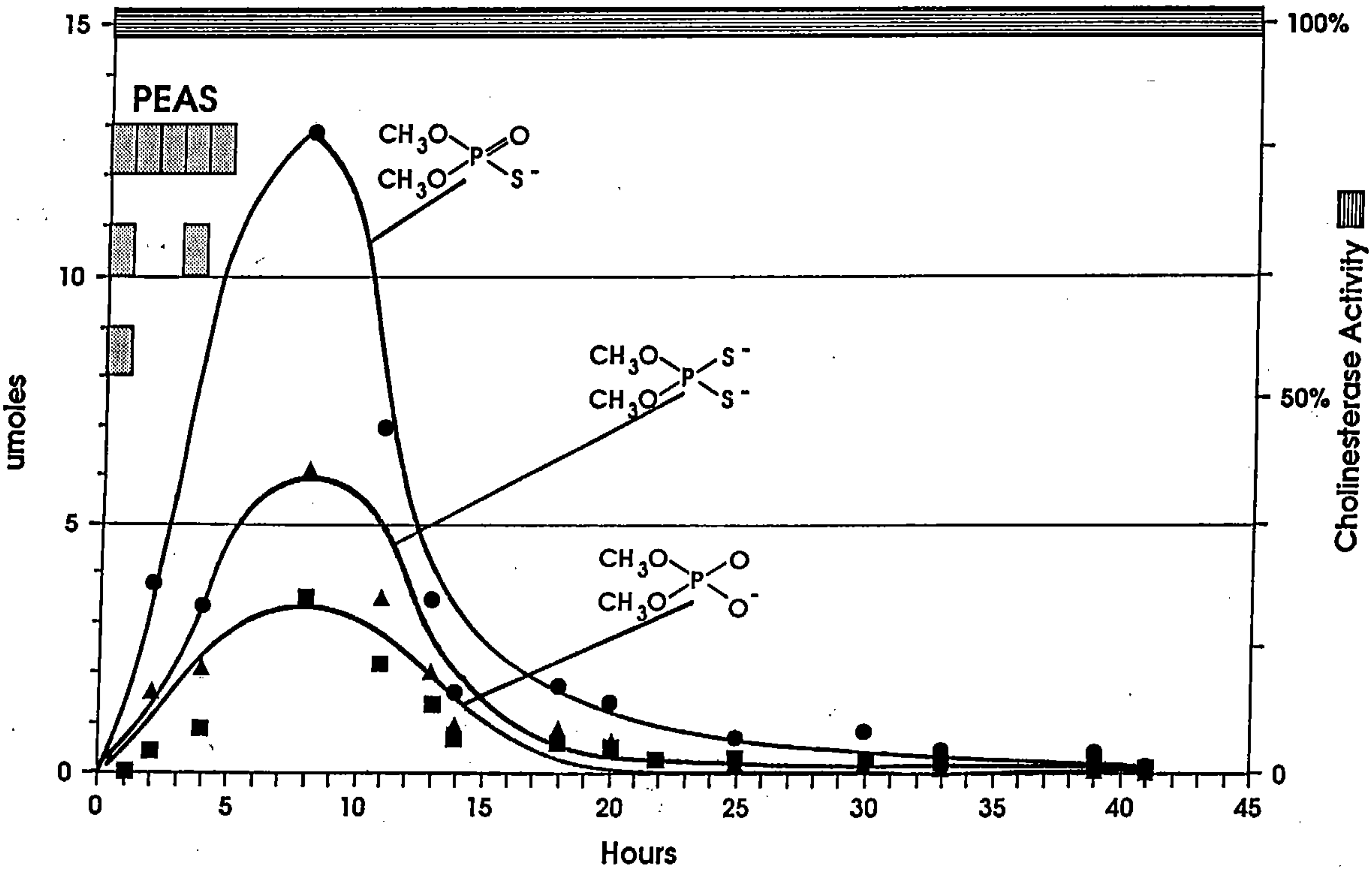


DMP



O-methoate

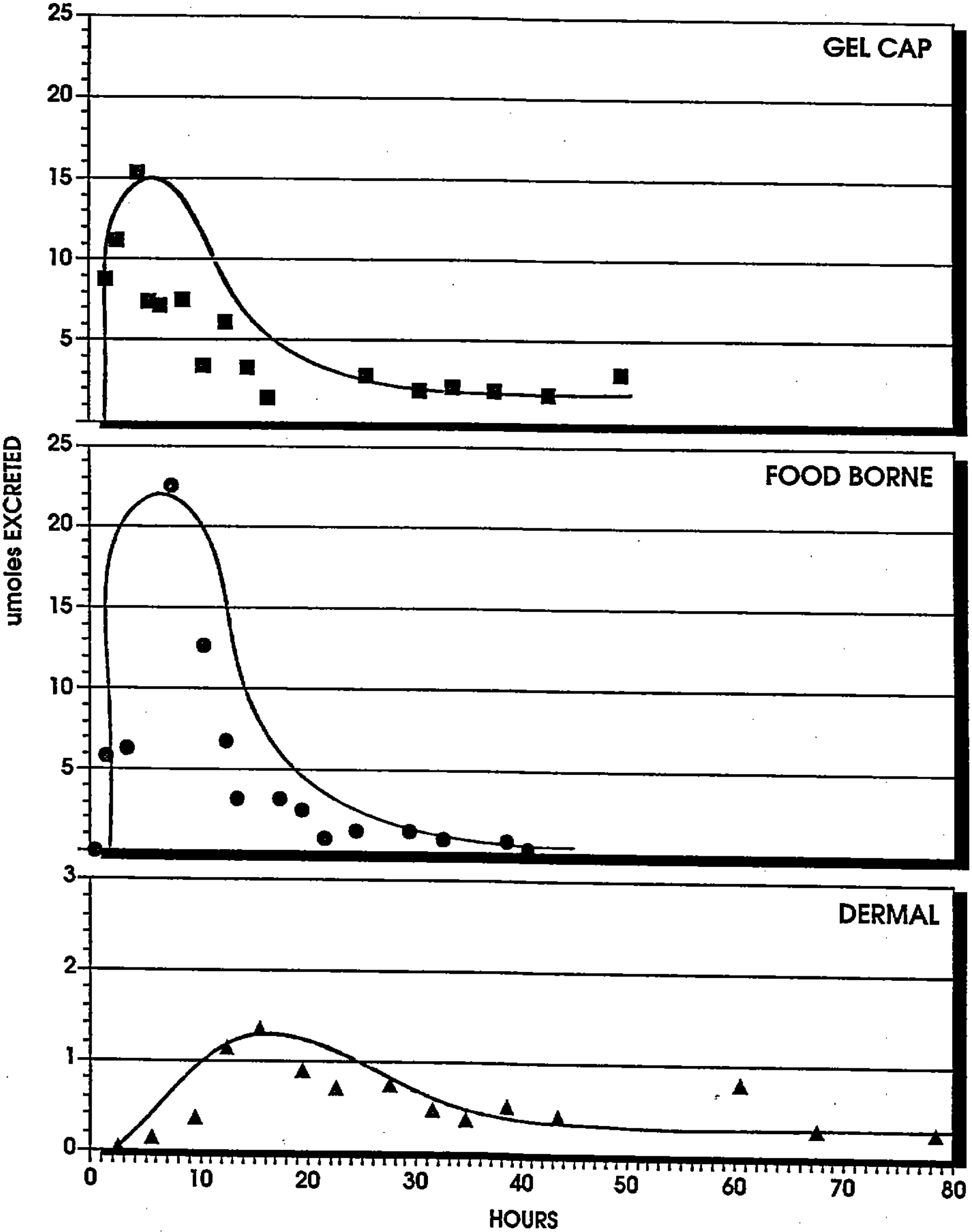
Urinary metabolites and dimethoate are shown above. In the time course shown below the relationship between the metabolites is shown: DMTP>DMDTP>DMP (oxon 0.16 µmoles and small amounts of dimethoate 0.07 µmoles not shown). On a molar basis, the metabolites (not corrected for recovery) accounted for nearly the entire dimethoate exposure. Corrected results exceeded exposure. Rapid metabolism of dimethoate and urinary excretion are clearly evident in this case.



Excretion of Dialkylphosphates in Urine After Ingestion

In corollary studies alkylphosphates (μmoles) were monitored following self-administration of dimethoate via the oral (gel cap; 20.2 mg; 0.14 mg/kg) and dermal (1.3 mg/kg; 1.95 mg/cm^2). The elimination profiles from urine are shown below. The profiles for metabolites following gel cap and food borne are strikingly similar. When examined in greater detail, absorption of the food borne residue was prolonged by the five-hour period during which ingestion occurred. Dermal absorption was substantially less (1 per cent or less) than uptake following gel cap or food borne exposures at similar dosages (0.14 vs. 0.12). Recoveries as alkylphosphate were 96 and 90 percent, respectively.

No toxic effects were observed in any case. Red blood cell acetylcholinesterase yielded no indication of dimethoate exposure.



DIMETHOATE METABOLITES IN URINE

CONCLUSIONS

1. Situational Chemical Exposure Studies can yield valuable perspectives concerning dose for human exposure assessments and risk management.

2. Examples of important insight from present studies include:

   A. Chlorpyrifos is probably biologically insignificant in homes following use of home foggers.

   B. Dimethoate is extremely rapidly eliminated in urine following ingestion of over tolerance (16 ppm vs 2 ppm) snow peas. In this case there is clearly no relationship between the food tolerance (an agricultural issue) and food safety (a complex health issue).

   C. Malathion dusts in date palm gardens result in more extensive malathion exposure of applicators and harvesters than previously estimated (exposure levels remain below toxic thresholds). Inhalation/ingestion may be contributing more substantially to exposure than previously recognized.

3. Unanticipated opportunities to monitor human chemical exposures are facilitated by readily available sensitive instrumental analytical methods.